Clinical trial results:
A Single Country, Multicenter, Open-Label and Non-Randomized Clinical Trial With Nonacog Alfa Prophylaxis and Treatment of Bleeding Episodes in Previously Treated Patients With Moderately-Severe to Severe Hemophilia B for a Duration of 8 Weeks

Summary

EudraCT number	2020-004430-38
Trial protocol	Outside EU/EEA
Global end of trial date	24 September 2020

Results information

Result version number	v1 (current)
This version publication date	17 March 2021
First version publication date	17 March 2021

Trial information

Trial identification

Sponsor protocol code	B1821059

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the safety of nonacog alfa when administered for prophylaxis with respect to incidence of factor IX (FIX) inhibitor development.

Protection of trial subjects:

The study was conducted in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 February 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	India: 25
Worldwide total number of subjects	25
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	3
Adults (18-64 years)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in India from 10 Feb 2020 to 24 Sep 2020. A total of 25 subjects were enrolled.

Pre-assignment

Screening details:

In this study, subjects aged greater than or equal to (>=) 12 years to less than or equal to (<=) 65 years, congenital moderately-severe to severe hemophilia B (FIX activity less than or equal 2 percent) who had at least 50 exposure days (EDs) to FIX-containing products were enrolled.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Nonacog alfa

Arm description:

Subjects received nonacog alfa intravenous (IV) injection as follows: Prophylactic treatment regimen: at a dose of 40 international unit per kilogram (IU/kg) (range 13 to 78 IU/kg) at intervals of 3 to 4 days in accordance with the local product document (LPD) guidelines until at least 16 exposure days or a period of up to 8 weeks on nonacog alfa treatment had occurred (whichever occurred first). For on demand (OD)treatment (infusions used to treat bleeding episodes) regimen nonacog alfa was administered at individual doses and frequency depending on the clinical effectiveness in individual subjects as recommended in approved LPD.

Arm type	Experimental
Investigational medicinal product name	Nonacog alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received nonacog alfa at a dose of 40 IU/kg (range 13 to 78 IU/kg) for up to 8 weeks or until 16 exposure days, whichever occurred first.

Number of subjects in period 1	Nonacog alfa
Started	25
Completed	25

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	25	25	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	3	3	
Adults (18-64 years)	22	22	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	28.44		
standard deviation	± 10.96	-	
Gender Categorical Units: Subjects			
Female	0	0	
Male	25	25	
Race (NIH/OMB) Units: Subjects			
Asian	25	25	
Ethnicity (NIH/OMB) Units: Subjects			
Not Hispanic or Latino	25	25	

End points

End points reporting groups

Reporting group title	Nonacog alfa

Reporting group description:

Subjects received nonacog alfa intravenous (IV) injection as follows: Prophylactic treatment regimen: at a dose of 40 international unit per kilogram (IU/kg) (range 13 to 78 IU/kg) at intervals of 3 to 4 days in accordance with the local product document (LPD) guidelines until at least 16 exposure days or a period of up to 8 weeks on nonacog alfa treatment had occurred (whichever occurred first). For on demand (OD)treatment (infusions used to treat bleeding episodes) regimen nonacog alfa was administered at individual doses and frequency depending on the clinical effectiveness in individual subjects as recommended in approved LPD.

Primary: Percentage of Subjects who Developed Factor IX (FIX) Inhibitors

End point title	Percentage of Subjects who Developed Factor IX (FIX) Inhibitors[1]

End point description:

FIX inhibitor development was defined as an inhibitor titer >= 0.6 Bethesda units per milliliter (BU/mL) confirmed by central laboratory testing during the course of the study. Safety analysis set included all subjects who received at least one dose of nonacog alfa.

End point type	Primary

End point timeframe:

At Visit 4 (any 1 day between Day 52 to Day 60)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percentage of subjects				
number (confidence interval 90%)	0 (0.00 to 0.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs) and Medically Important Events (MIEs)

End point title	Number of Subjects With Serious Adverse Events (SAEs) and Medically Important Events (MIEs)

End point description:

An AE is any untoward medical occurrence in clinical investigation subject administered a product or medical device; event need not necessarily to have a causal relationship with treatment or usage. SAEs: an AE resulting in any of following outcomes/deemed significant for any other reason: death; initial/prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. MIEs: any confirmed FIX inhibitor development (titer greater than or equal to 0.6 BU/mL confirmed by central laboratory testing), thrombotic events (any event associated with the formation of a blood clot including catheter-associated

thrombi and thrombotic complications) and hypersensitivity reactions (hypersensitivity reaction to an FIX product with symptoms such as hives, urticaria, tightness of chest, wheezing, hypotension, and anaphylaxis based on investigator's judgment). Safety analysis set.

End point type	Secondary

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 116 days)

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Subjects				
SAEs	0			
MIEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Treatment emergent are events between first dose of study drug and up to 28 days (up tp 116 days) that were absent before treatment or that worsened relative to pretreatment state. Safety analysis set included all subjects who received at least one dose of nonacog alfa.

End point type	Secondary

End point timeframe:

Baseline up to 28 days after last dose of study drug (up to 116 days)

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualized Bleeding Rate (ABR)

End point title	Mean Annualized Bleeding Rate (ABR)

End point description:

ABR: number of bleeding episodes per year. ABR for each subject = number of bleeds during treatment interval duration (TID)/(TID/365.25). Number of bleeds for each subject for ABR included all new bleeds (with unique start date and time) requiring treatment with nonacog alfa during TID. TID=date of Visit 4 (3-10 days after last dose) – date of Visit 2 (Day 1) +1. For subjects who had Visit 4 beyond 3 (+7) days after final dose due to COVID-19 pandemic, date of final dose was used in place of date of Visit 4. For discontinued subjects, date of final dose/last study visit date (whichever occurred later) was used to replace Visit 4. The overall mean ABR was calculated on all subjects from the safety analysis set who either received an on-demand infusion of Nonacog-Alfa due to a new bleed or did not had any bleed which required on-demand infusion with study drug.

End point type	Secondary

End point timeframe:

Up to 88 Days

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Bleeding episodes per year				
arithmetic mean (standard deviation)	()			

Notes:

[2] - Data not reported as no subject required and received OD treatment with study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualized Total Factor Consumption (TFC) per Subject

End point title	Mean Annualized Total Factor Consumption (TFC) per Subject

End point description:

The TFC per subject was the sum of the total amount in international units (IU) infused for each infusion for each subject. Annualized TFC of nonacog alfa was derived for each subject by using the following formula; Annualized TFC = (TFC / treatment interval duration)*365.25. Treatment interval duration was calculated as the number of days beginning on Visit 2 (“Day 1”, provided an infusion was given) up to Visit 4 (any 1 day between Day 52 to Day 60). Safety analysis set included all subjects who received at least one dose of nonacog alfa.

End point type	Secondary

End point timeframe:

Up to 88 Days

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: International units per subject				
arithmetic mean (standard deviation)	224582.44 (± 75526.750)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Annualized Total Factor Consumption (TFC) by Weight per Subject

End point title	Mean Annualized Total Factor Consumption (TFC) by Weight per Subject

End point description:

The total amount in international units (IU) infused for each infusion recorded were summed to calculate the total factor consumption for each subject. Annualized TFC = (TFC / treatment interval duration)*365.25. Treatment interval duration was calculated as the number of days beginning on Visit 2 ("Day 1", provided an infusion was given) up to Visit 4 (any 1 day between Day 52 to Day 60). Safety analysis set included all subjects who received at least one dose of nonacog alfa. International unit per kilogram= IU/kg.

End point type	Secondary

End point timeframe:

Up to 88 Days

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: IU/kg per subject				
arithmetic mean (standard deviation)	3639.27 (± 572.778)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Number of Nonacog Alfa Infusions Used to Treat Each Bleed

End point title	Mean Number of Nonacog Alfa Infusions Used to Treat Each Bleed

End point description:

Number of nonacog alfa infusions used to treat each bleed was calculated by adding the initial (on-demand) infusion to any subsequent (on-demand) infusions for the same bleed (same bleed start date/time). On demand treatment was defined as treatment used to treat a bleeding episode. Safety analysis set included all subjects who received at least one dose of nonacog alfa. Here, "Number of Subjects Analysed" signifies subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 88 days

End point values	Nonacog alfa			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Infusion				
arithmetic mean (standard deviation)	()			

Notes:

[3] - Data not reported as no subject was analysed with nonacog alfa infusion used to treat each bleed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 28 days after last dose of study drug (maximum up to 116 days)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Nonacog alfa

Reporting group description:

Subjects received nonacog alfa IV injection as follows: Prophylactic treatment regimen: at a dose of 40 IU/kg (range 13 to 78 IU/kg) at intervals of 3 to 4 days in accordance with the LPD guidelines until at least 16 exposure days or a period of up to 8 weeks on nonacog alfa treatment had occurred (whichever occurred first). For on demand (OD) treatment (infusions used to treat bleeding episodes) regimen nonacog alfa was administered at individual doses and frequency depending on the clinical effectiveness in individual subjects as recommended in approved LPD.

Serious adverse events	Nonacog alfa		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Nonacog alfa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 25 (12.00%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported